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Dear Mather-

It was very gratifying indeed to receive your recent letter; Your discussions with me have had a very beneficent effect in clarifying what I must do, and I hope your interest in this problem will continue. The results so far have satisfied the criteria a, b, and c which you mentioned. I had just completed my own analysis of the data which I had sent you with substantially the same results. In addition, I have estimated the homogeneity of the various samples. Parts of Sets 2 and 4 give 'p's of .04 and .06 respectively, for reasons which I am at a loss to assign, so that it is if anything remarkable how well the data for 'coupling' and repulsion phases fit; for sets 1-4 respectively (with some new data) the 'p's are .005, 0.3, 0.18, .02, which are commensurate with the homogeneity of the data.

While the 4 sets were chosen from the point of view of the cycle: BM, BØC, TP, TLB_1, I had been so pessimistic about the possibility of an effect of both BØC/BM and TP/TLB_1 that I had not gotten to sit down and analyse the data. The lack of effect of the first substitution is surprising, but seems to be authenticated by the data; thank you very much for pointing this out to me, and for showing how the frequency of the 4th rare recombination class of set 4. can be used to estimate the absolute distance (although inefficiently On the basis of the comparison of the number of colonies which appear on minimal and and TL agar in the $BMTLB_1$ cross, I had come to the comclusion that the distance BM--TL was from 70-90 units.

Since distances of more than 50 units are certainly involved, it is now of crucial importance to determine whether criteria for a 2- or 4-strand system can be elaborated; results so far are ambiguous.

It is surprising that only one linkage group has been uncovered, but that seems to be the situation. I think the possibility of spurious linkages (like B.....M) in your notation has been covered.

There is one interpretation with which I should like to take issue: '..we must assume that T_1 is linked to L and P rather than to T.... T..must be further from T_1 than L and P are.' If P,T and L are in linear order (not necessarily this one), T_1-P-T would show a smaller recombination frequency than T_1-TL, regardless of the order of T and L. In a sense, P masks whatever is beyond it. On this theory the map should be

$$B_1^{+}\text{---}\underset{-}{\underset{-}{BM}}\text{-----Lac---------}\overset{+}{V}\text{---P---}\underset{+}{\underset{+}{TL}}.$$

Fortunately, we have the mutant B^-P^-, so that we can perform the cross: B_1+B-Lac+V^SP-T+L+ X ..-+-r+--. The results of the segregations of Lac and V in the prototroph, B_1^- and B^- classes should provide material for a confirmation (or refutation) of our previous hypotheses.

The question of the relationship between T and L can be best examined in the cross B-T-V^r X L-B_1-V^S, simply by studying the segregation of V into the prototrophs. I hope to have more definite information in a few weeks. Till then, with best regards,

Yours sincerely,

Joshua Lederberg.